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(54) Neuromodulatory peptide.

(57) Peptide having the formula:
gly pro glu; gly pro; pro glu; ala gly pro; ala gly; gly pro glu thr; pro glu thr; glu thr, optionally blocked at one or both of the N- and C-terminals thereof;
the medicinal or diagnostic use of such peptide; and a composition for medicinal or diagnostic use comprising an active amount of such peptide.

Fig. 1

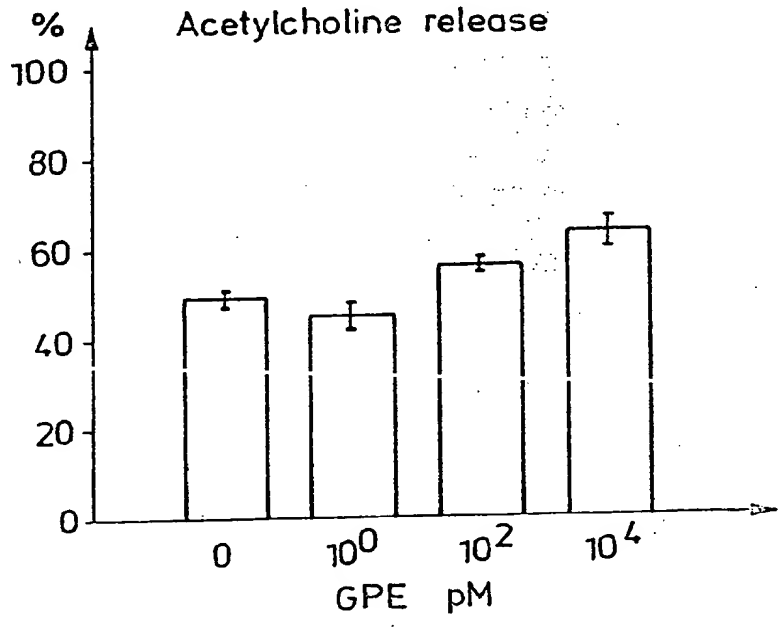

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Fig. 2 illustrates stimulation and inhibition of cortical neurone activity upon administration of the peptide of the invention; and

Fig. 3 is a diagram illustrating the electrophysiological reflex response in the spinal cord upon administration of the peptide.

EXAMPLE 1

The tripeptide glycylprolylglutamic acid (H_2N-Gly-Pro-Glu-COOH) was synthesized according to the stepwise solid phase technique (Kent, S.B.H. (1988) Ann.Rev.Biochem. 57, 957-989) in an Applied Biosystems Model 430 A peptide synthesizer. A phenylacetamidomethyl (PAM) resin was used as the solid support and the following tert-butyloxycarbonyl (tBoc) amino acid derivatives were employed: L-Glu-benzyl ester (OBzl), L-Pro and Gly. A standard program including pre-formation of symmetric anhydrides was used for the synthesis. The resulting peptide was cleaved from the resin and deprotected by the hydrogen fluoride (HF) method and subsequently purified by reverse phase high performance liquid chromatography (HPLC). The identity and purity of the final product was assessed by amino acid analysis.

EXAMPLE 2

The tripeptide resulting from the manufacture according to Example 1 above was used in a test system according to L. Nilsson, V.R. Sara and A. Nordberg, Neurosience Letters, 1988, Vol. 88, pp 221-226. This test procedure is based on stimulation of the release of acetylcholine from cortical brain slices. The results of this experiment is shown in Fig. 1, wherein the tripeptide's ability to inhance the release of acetylcholine from neurones following depolarization is shown.

EXAMPLE 3

The tripeptide from Example 1 above was used in modulation of the electrophysiological activity of cortical neurones, and the results of this experiment is illustrated in Fig. 2. As can be seen from Fig. 2 the tripeptide both stimulates and inhibits cortical neurone activity and modulates the neural response to neurotransmitters. In this experiment the procedure according to T.W. Stone (Ed.), "Microiontophonesis and pressure ejection", John Wiley & Sons, New York, 1985 was used.

EXAMPLE 4

Following the procedure of Z. Wiesenfeld-Hallin, Bruin Research 372:172-175, 1986, experiments were performed, wherein the tripeptide of Example 1 was shown to facilitate the electrophysiological reflex response in the spinal cord.

The result of these experiments is shown in Fig. 3, from which it is clear that the tripeptide increases both the peak and the duration of th reflex response.

Claims

1. Peptide for medicinal or diagnostic use, characterized by the formula:
gly pro glu; gly pro; pro glu; ala gly pro; ala gly; gly pro glu thr; pro glu thr; glu thr, optionally blocked at one or both of the N- and C-terminals thereof.

2. Peptide according to claim 1, characterzied by the formula:
gly pro glu; gly pro; or pro glu.

3. Peptide according to claim 2 having the formula:
gly pro glu.

4. Peptide according to any preceding claim for use as a neuromodulator.

5. Peptide according to claim 4 for use in the treatment of disorders of the nervous system.

6. Peptide according to claim 4 for use in the treatment of senile dementia.

7. Peptide according to any preceding claim for use in the treatment of psyciatric disorders.

8. A composition for medicinal use comprising an active amount of a peptide according to any preceding claim in combination with a therapeutically acceptable carrier therefor.

9. A composition for diagnostic use comprising an active amount of a peptide according to any of claims 1 to 3 in combination with a diagnostically acceptable carrier therefor.

10. A composition according to claim 8, wherein said carrier is adapted for nasal administration.

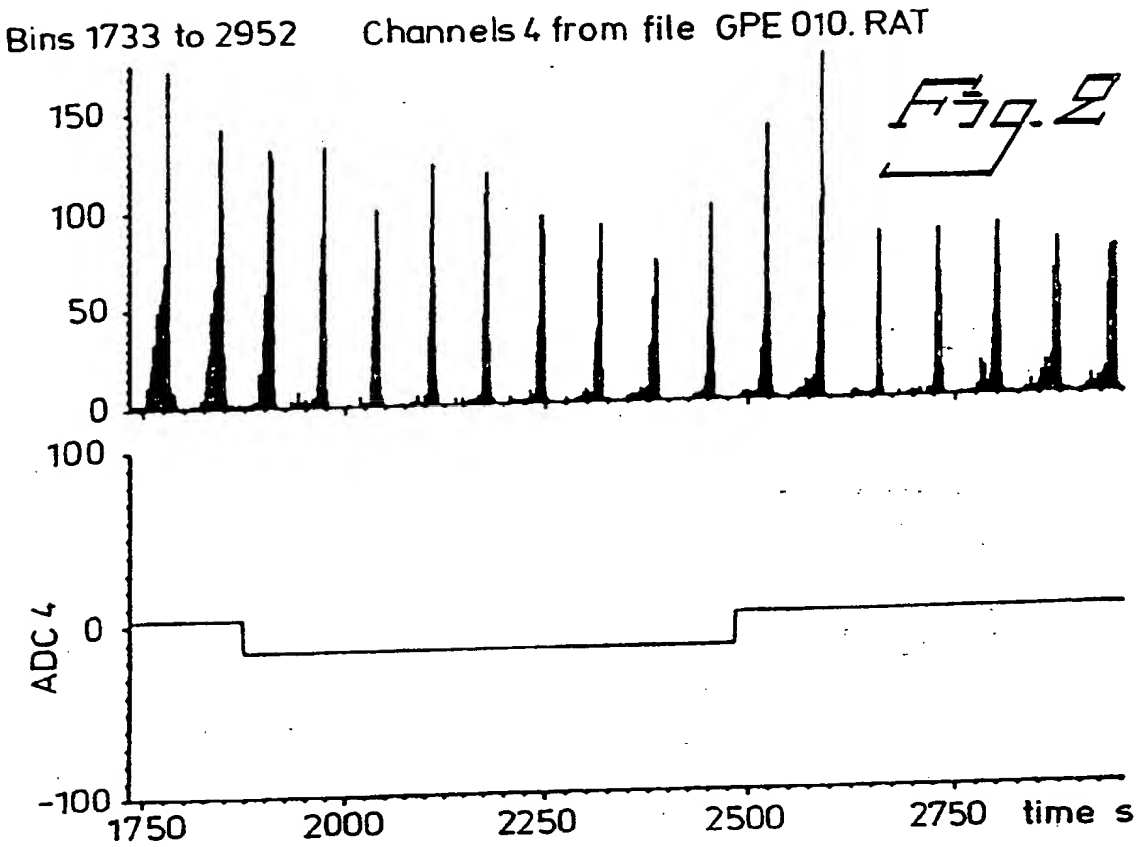

Fig. 2

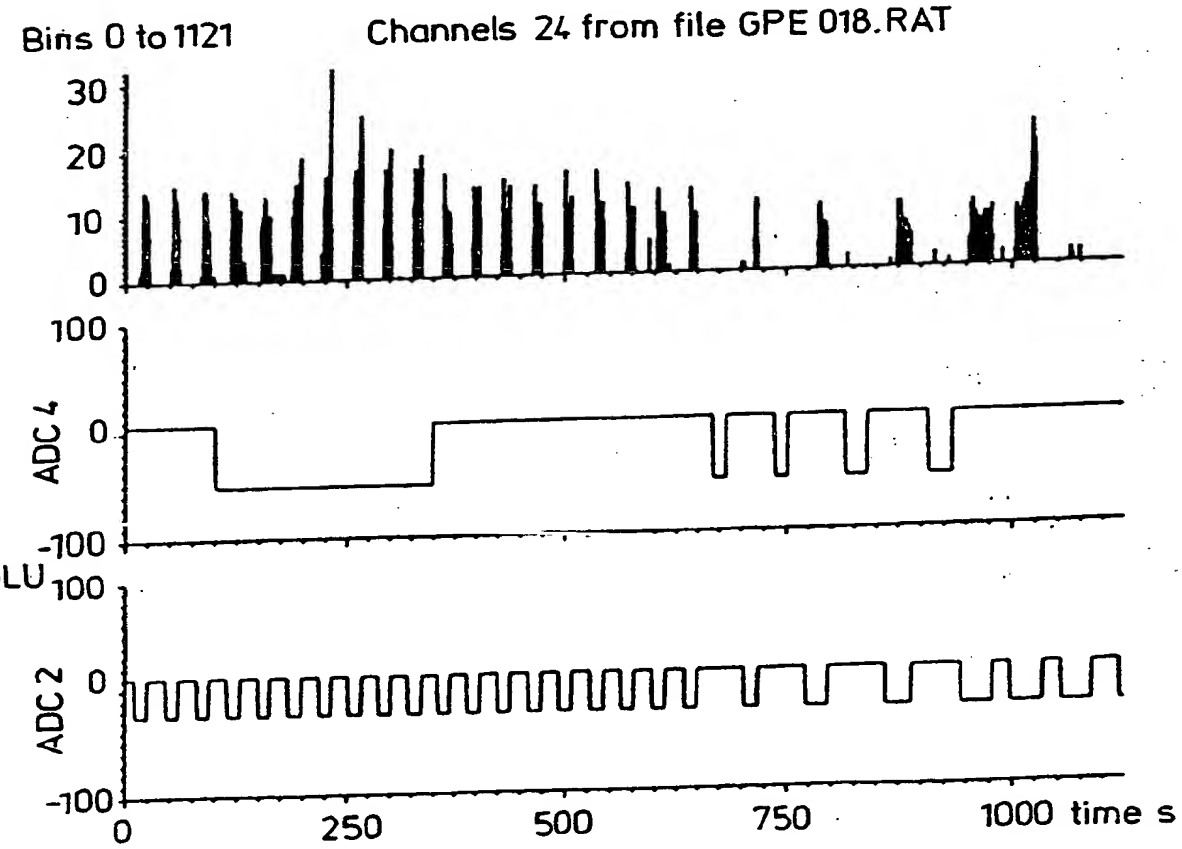

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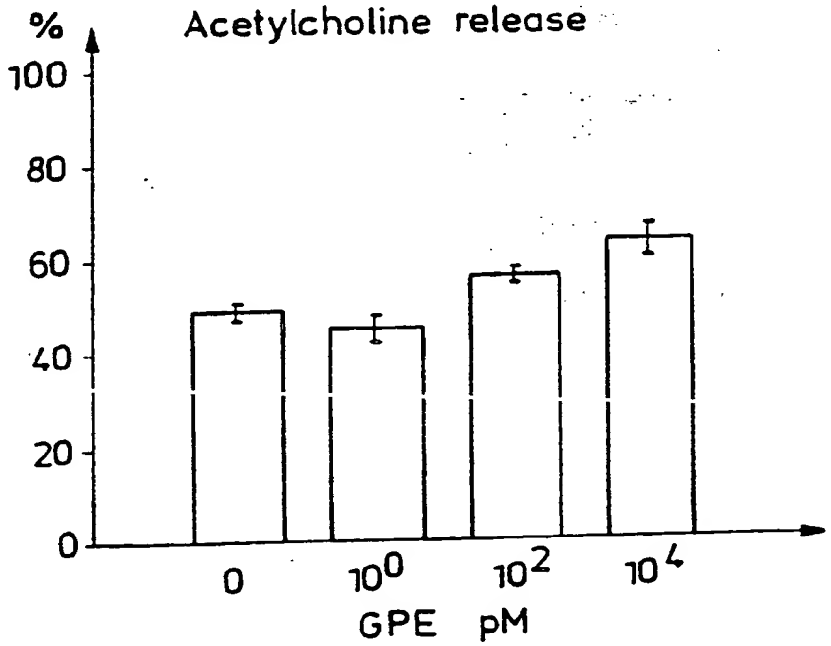
Fig. 1



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